

Flow Chart: Schedule of Study Events

	Pre-Treatment Period	Treatment Period				Observation Period				
	Visit 1 (Weeks -12 to 0)	Visit 2 Week 0 (Day 0)	Visit 3 Week 3	Visit 4 Week 6	Visit 5 Week 10	Visit 6 Week 14	Visit 7 Week 18	Visit 8 Week 22	Visit 9 Week 26	Visit 10 2-4 weeks Post-LEEP
Activity										
Inclusion/Exclusion criteria satisfied	X									
Informed Consent signed	X									
Confirm CIN II/III by colposcopy <sup>a</sup>	X									
Confirm Medical History	X								X	
Complete Physical Examination	X									
Symptom-directed physical examination <sup>b</sup>		X	X	X	X					
Vital Signs	X	X <sup>c</sup>	X <sup>c</sup>	X <sup>c</sup>	X					
Hematology, chemistry, urinalysis	X							X	X	X
HBV and HCV testing	X									
Pregnancy Test (HCG in urine)	X	X	X	X						
Pelvic and colposcopic examination	X	X <sup>d</sup>	X	X	X	X	X	X	X	
Pap test cytology	X			X	X		X		X	
HPV testing (presence/absence)	X <sup>e</sup>			X	X		X		X	
HPV typing (by PCR)	X			X	X		X		X	
T4 and TSH testing	X				X				X	
Immunology blood samples (drawn before dosing at Weeks 0, 3, and 6)		X	X	X	X	X	X	X	X	
ZYC101a Injection (7-day window)		X	X	X						
Local tolerability assessment		X <sup>f</sup>	X <sup>f</sup>	X <sup>f</sup>	X					
Adverse event monitoring		X	X	X	X	X	X	X	X	
Concomitant medications review	X	X	X	X	X	X	X	X	X	
LEEP or equivalent procedure; histopathology on tissue samples				X <sup>g</sup>	X <sup>g</sup>	X <sup>g</sup>	X <sup>g</sup>	X <sup>g</sup>	X <sup>g</sup>	
Pharmacoeconomic data collection	X									X <sup>i</sup>

a. Confirmation of CIN II/III by colposcopy occurred between the time of biopsy and the first injection of ZYC101a, and did not exceed 12 weeks.

b. Physical examination was directed to any areas of complaints or findings.

c. Vital signs were taken before dosing and at 15, 30, and 60 minutes after dosing.

d. Colposcopic exam could be waived at Visit 2, if it occurred within 4 weeks of Visit 1.

e. HPV typing at Visit 1 occurred within 12 weeks of diagnosis of CIN II/III.

f. Local tolerability was re-evaluated at 24 hours after dosing.

g. LEEP or cold knife cone was performed on progressive lesions. Safety assessments were performed for 6 months from the time of the first injection of study drug.

h. LEEP or cold knife cone was performed on all lesions at 6±1 months after the first injection of study drug. Safety assessments were performed before the LEEP.

i. Pharmacoeconomic data were collected 2 or 4 weeks after the LEEP was performed, even if performed early.

Fig. 1

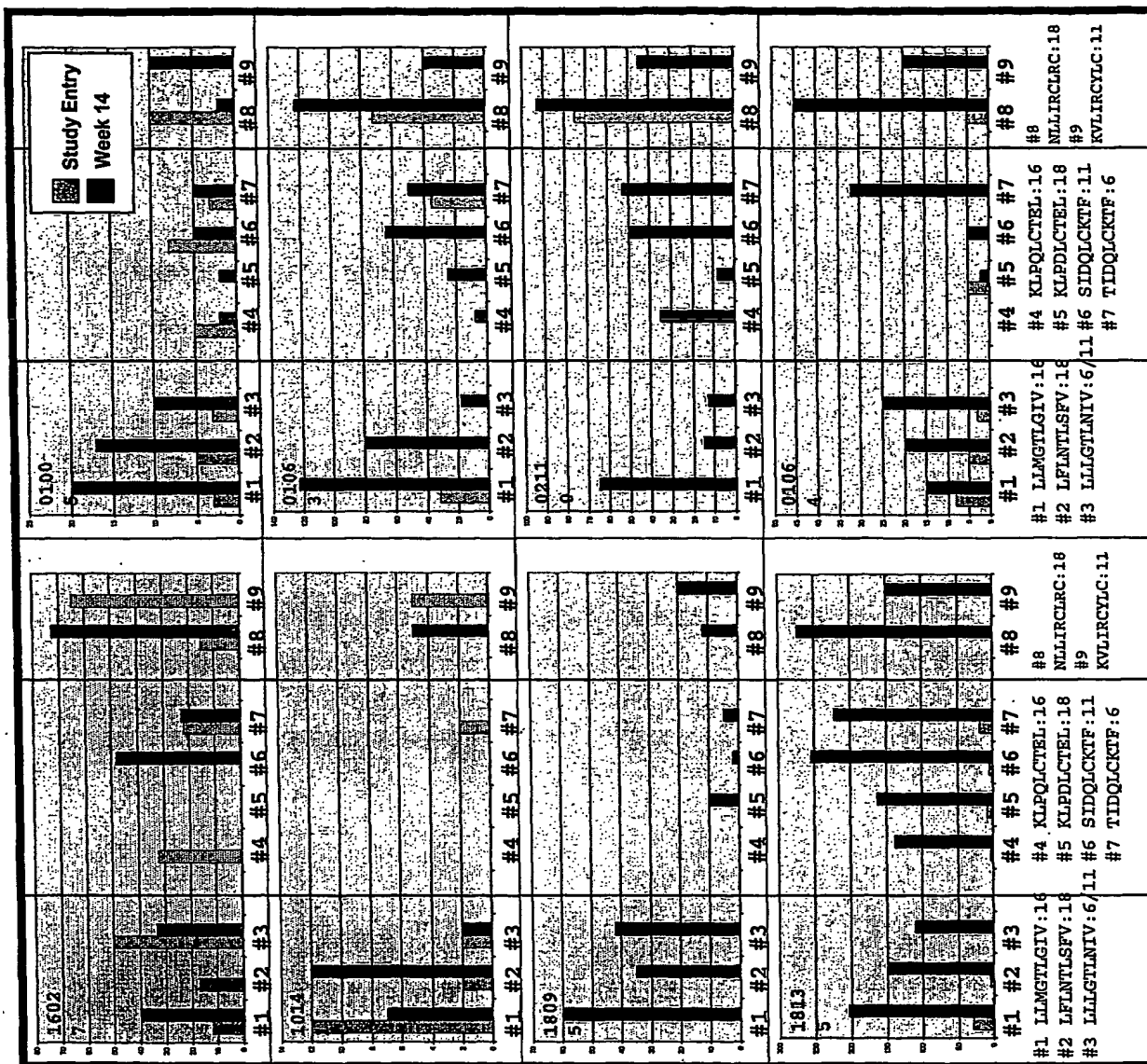


Fig. 2

Change in Tumor Size in TC-1 #6

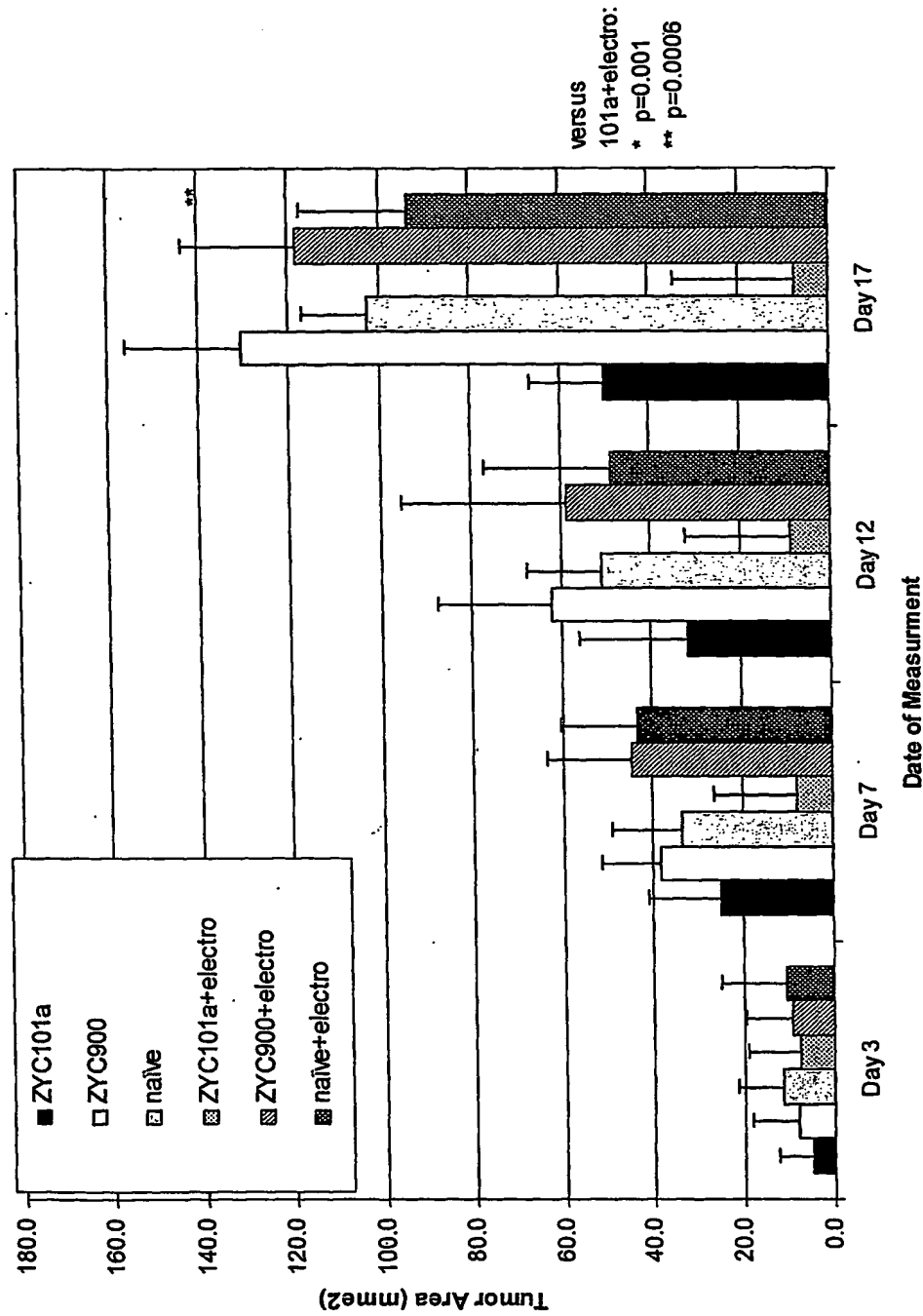


Fig. 3